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APPLICATION NO	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO	CONFIRMATION NO
09/856,070	05/17/2001	Rupert Donald Holmes	GJE-67	5703

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EXAMINER	
KAM, CHIEH MIN	

ART UNIT	PAPER NUMBER
1653	13

DATE MAILED: 04/04/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/856,070	HOLMS, RUPERT DONALD	
	Examiner	Art Unit	
	Chih-Min Kam	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 December 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *31-34,36 and 50-66* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *31-34,36 and 50-66* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4* .
4) ☒ Interview Summary (PTO-413) Paper No(s). *13* .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Applicant's election of Group I, claims 31-66 and SEQ ID NO:19 in Paper No. 9 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). However, upon reconsideration, the amino acid sequences (SEQ ID NOs:2 and 16-27 cited in claim 34) encompassed in the residues 333-373 of the Hepreceptor will be examined. In the preliminary amendment filed December 30, 2002 (Paper No. 9), claims 35, 37-49 and 67-76 have been cancelled, and claims 31-34 have been amended. Therefore, claims 31-34, 36 and 50-66, along with SEQ ID NOs: 2 and 16-27 are examined.

Sequence Listing

2. The amendment on sequence listing filed February 11, 2003 is acknowledged, and CRF has been entered. In the newly submitted sequence listing, SEQ ID NO:2 is the amino acid sequence of residues 340-373 of Hepreceptor, where Xaa at position 14 is phosphorylated tyrosine. However, the amino acid sequence of residues 340-373 of Hepreceptor with Xaa = Tyr is not included in the sequence listing. To advance prosecution, a telephone call was made to David Saliwanchik on March 31, 2003 to modify SEQ ID NO:2 in the sequence listing (see interview summary), Xaa = Tyr(P) at position 14 has been changed to Xaa = Tyr(P) or Tyr.

Informalities

3. The disclosure is objected to because of the following informalities:

At page 3, last paragraph, it appears the reasoning for anti-HIV effect of HEP1 is not fully described. Appropriate correction is required.

Claim Objections

4. Claim 66 is objected to because the claim contains non-elected sequences, e.g., SEQ ID NOs:1 and 3-15.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

5. Claims 31-34, 36 and 50-61 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The claim is drawn to a molecule which is a peptide. As written, the claim does not explicitly indicate the hand of man. Insertion of "isolated", "purified" or "synthetic" in connection with a molecule is suggested. See MPEP § 2105.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 62-66 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of upregulating the immune system in a patient with an identified disease (e.g., cancer, HIV, or bacteria infection) in need of such regulation, comprising administering a Hepreceptor peptide having a defined amino acid sequence, does not reasonably provide enablement for a method for upregulating the immune system in a patient in need of such regulation, comprising administering a molecule which binds to the Hepreceptor, where the disease state of the patient and the structure of the molecule are not defined. The specification

does not enable a person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Claims 62-66 are directed to a method for upregulating the immune system in a patient in need of such regulation, comprising administering a molecule which binds to the Hepreceptor (claims 62, 63), or administering a molecule comprising an amino acid sequence identical to all or part of the Hepreceptor (claims 64-66). The specification, however, only discloses cursory conclusions without data supporting the findings, which states that any charged molecule that partially mimics the interaction between the sides chains of Domain A and Domain B of the Hepreceptors will stimulate immune response by binding to the Hepreceptor, a novel active site in human ezrin) (page 3, paragraph 1; page 8 paragraph 1). There are no indicia that the present application enables the full scope in view of the method for upregulating the immune system in a patient using a molecule which binds to the Hepreceptor as discussed in the stated rejection. The present application provides no indicia and no teaching/guidance as to how the full scope of the claims is enabled. The factors considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F2d at 731,737, 8 USPQ2d at 1400,1404 (Fed. Cir.1988)). The factors most relevant to this rejection are the breath of the claims, the absence of working examples, the state of the prior art and relative skill of those in the art, the unpredictability of the art, the nature of the art, the amount of direction or guidance presented, and the amount of experimentation necessary.

(1). The breath of the claims:

The breath of the claims is broad and encompasses unspecified variants regarding the molecule which binds to the Hepreceptor, and the disease state of the patient, which are not adequately described or demonstrated in the specification.

(2). The absence or presence of working examples:

There are working examples indicating Hepreceptor peptide with a defined sequence activates the immune system in patients with HIV (Example 3), reduces the growth rate of tumor cells (Example 2), or stimulates the immune response in patients with microbial infection (Examples 4, 9 and 10). However, there are no working examples demonstrating the use of molecules other than Hepreceptor peptides in the methods of upregulation of immune system in patients in need of such regulation.

(3). The state of the prior art and relative skill of those in the art:

The prior art (Holms, U. S. Patent 5,773,573) indicates HEP1 (TEKKRRETEREKE, residues 324-337 of human ezrin) can inhibit HIV replication in vivo. However, the general knowledge and level of the skill in the art do not supplement the omitted description, the specification needs to provide specific guidance on identities of the molecules other than Hepreceptor peptides and the disease states of patients in need of such regulation, and the effects of the molecules in upregulation of immune system to be considered enabling for variants.

(4). Predictability or unpredictability of the art:

The claims encompass a method for upregulating the immune system in a patient in need of such upregulation, comprising administering a molecule which binds to the Hepreceptor. However, the specification does not identify any molecules other than Hepreceptor peptides, nor indicates the effect of the molecule for upregulating the immune system in a patient where the

disease state is not specified, the invention is highly unpredictable regarding the outcome of the treatment using molecules which are not identified.

(5). The amount of direction or guidance presented and the quantity of experimentation necessary:

The claims are directed to a method for upregulating the immune system in a patient in need of such upregulation, comprising administering a molecule which binds to the Hepreceptor. The specification indicates Hepreceptor peptides activate the immune system in patients with HIV (Example 3), reduce the growth rate of tumor cells (Example 2), and stimulate the immune response in patients with microbial infection (Examples 4, 9 and 10). However, the specification does not provide any specific guidance on how to identify a patient in need of such upregulation without indicating the disease state of the patient. Furthermore, the specification has not identified any molecule other than Hepreceptor peptides, which binds to Hepreceptor, nor has demonstrated the use of the molecules in the treatment. There are no working examples indicating the effects of the molecules in upregulating the immune system in a patient in need of such upregulation. Since the specification has not provided sufficient teachings on identities of the molecules and the treating conditions such as the dose and the time for the patient in need of such upregulation but the disease state is not identified, thus, it is necessary to have additional guidance on the structures of the molecules other than Heprecptor peptides, and the treatment of patients in need of such upregulation, and to carry out further experimentation to assess the effect of the molecule in the treatment.

(6). Nature of the Invention

The scope of the claims encompass a method for upregulating the immune system in a patient by administering a molecule which binds to the Hepreceptor, but the specification only shows the Heprecptor peptides activate the immune system in patients with an identified disease, it has not demonstrated the use of any molecule other than Heprecptor peptides in activation of immune system in a patient in need of such upregulation. Thus, the disclosure is not enabling for the reasons discussed above.

In summary, the scope of the claim is broad, while the working example does not demonstrate the claimed variants, the outcome of treatment is unpredictable using the claimed variants, and the guidance and the teaching are limited, therefore, it is necessary to have additional guidance and to carry out further experimentation to assess the effect of the molecule in upregulation of immune system.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 31-33 and 62-66 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

7. Claims 31-33 and 64-65 are indefinite because of the use of the term "a portion" or "part". The term "a portion" or "part" renders the claim indefinite, it is unclear what amino acid sequence the portion of amino acid residues 333-373 of the Hepreceptor or the part of the Hepreceptor has. Claims 31 and 32 are also indefinite because the claim recites amino acid position(s) (e.g., amino acid residues 333-373 of the Hepreceptor) without reference to an amino

acid sequence identified with "SEQ ID NO:". It is not clear what the amino acid position is without a sequence identifier "SEQ ID NO:". Claims 33 and 65 are included in the rejection because they are dependent on a rejected claim and do not correct the deficiency of the claim from which they depend.

8. Claims 62-66 are indefinite because they lack essential steps as claimed in the process of upregulating the immune system. The omitted step is the outcome of the treatment. Claims 63-66 are included in the rejection because they are dependent on rejected claims and do not correct the deficiency of the claim from which they depend. Claims 62 and 63 are also indefinite because of the use of the term "a molecule". The term "a molecule" renders the claim indefinite, it is unclear what structure the molecule has.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (c) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

9. Claims 31-34, 50-53, 55, 57, 59 and 60 are rejected under 35 U.S.C. 102(b) as being anticipated by Gould *et al.* (The EMBO Journal 8, 4133-4141 (1989)).

Gould *et al.* teach the cloning of a human ezrin and the protein sequence derived from the nucleotide sequence of the cDNA and from partial direct protein sequencing, where the protein sequence contains EREKEQMMREKEELMLRLQDYEEKTKKAERELSEQIQRALQ (residues 333-373; Fig. 1, page 4134; claims 31-33, 50-53, 55, 57, 59 and 60).

10. Claims 31-34 and 50 are rejected under 35 U.S.C. 102(b) as being anticipated by Holms (US Patent 5,773,573).

Holms teaches a purified peptide, TEKKRRETVEREKE based on human ezrin is used for the treatment of AIDS (column 1, lines 61-65; column 3, lines 49-50; claims 31-34 and 50).

11. Claims 31-34, 36 and 50 are rejected under 35 U.S.C. 102(e) as being anticipated by Arpin *et al.* (U.S. Patent 6,399,584, filed on March 18, 1998).

Arpin *et al.* teach the amino acid sequence of ezrin, which contains EREKEQMMREKEELMLRLQDYEEKTKKAERELSEQIQRALQ (residues 333-373; Fig. 1A, SEQ ID NO:1 of the patent; claims 31-33, 50-53, 55, 57, 59 and 60), where Tyr145 located in the N-terminal domain and Tyr353 in the α-helical domain can be phosphorylated by EGF receptor (column 1, lines 36-44; claims 36, 54, 56, 58 and 61). The reference also teaches the amino acid sequence of RQIKIWFQNRRMKWKKLRLQDY(p)EEKTK (SEQ ID NO:2 of the patent; column 3, lines 1-3; claim 61).

Conclusion

12. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chih-Min Kam whose telephone number is (703) 308-9437. The examiner can normally be reached on 8.00-4:30, Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low, Ph. D. can be reached on (703) 308-2923. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-0294 for regular communications and (703) 308-4227 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Chih-Min Kam, Ph. D. C.T.K
Patent Examiner

***
March 31, 2003

Christopher S. F. Low
CHRISTOPHER S. F. LOW
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

Interview Summary	Application No.	Applicant(s)	
	09/856,070	HOLMS, RUPERT DONALD	
	Examiner	Art Unit	
	Chih-Min Kam	1653	

All participants (applicant, applicant's representative, PTO personnel):

(1) *Chih-Min Kam*. (3)_____.

(2) *David Saliwanchik*. (4)_____.

Date of Interview: *31 March 2003* .

Type: a)☒ Telephonic b)☐ Video Conference
c)☐ Personal [copy given to: 1)☐ applicant 2)☐ applicant's representative]

Exhibit shown or demonstration conducted: d)☐ Yes e)☐ No.
If Yes, brief description: _____ .

Claim(s) discussed: _____ .

Identification of prior art discussed: _____ .

Agreement with respect to the claims f)☐ was reached. g)☐ was not reached. h)☐ N/A.

Substance of Interview including description of the general nature of what was agreed to if an agreement was reached, or any other comments: *to amend SEQ ID NO:2 in sequence listing where Xaa =Tyr(P) has been changed to Xaa=Tyr(P) or Tyr* .

(A fuller description, if necessary, and a copy of the amendments which the examiner agreed would render the claims allowable, if available, must be attached. Also, where no copy of the amendments that would render the claims allowable is available, a summary thereof must be attached.)

THE FORMAL WRITTEN REPLY TO THE LAST OFFICE ACTION MUST INCLUDE THE SUBSTANCE OF THE INTERVIEW. (See MPEP Section 713.04). If a reply to the last Office action has already been filed, APPLICANT IS GIVEN ONE MONTH FROM THIS INTERVIEW DATE TO FILE A STATEMENT OF THE SUBSTANCE OF THE INTERVIEW. See Summary of Record of Interview requirements on reverse side or on attached sheet.

Examiner Note: You must sign this form unless it is an Attachment to a signed Office action.

Examiner's signature, if required

Summary of Record of Interview Requirements

Manual of Patent Examining Procedure (MPEP), Section 713.04, Substance of Interview Must be Made of Record
A complete written statement as to the substance of any face-to-face, video conference, or telephone interview with regard to an application must be made of record in the application whether or not an agreement with the examiner was reached at the interview.

Title 37 Code of Federal Regulations (CFR) § 1.133 Interviews
Paragraph (b)
In every instance where reconsideration is requested in view of an interview with an examiner, a complete written statement of the reasons presented at the interview as warranting favorable action must be filed by the applicant. An interview does not remove the necessity for reply to Office action as specified in §§ 1.111, 1.135. (35 U.S.C. 132)

37 CFR §1.2 Business to be transacted in writing.
All business with the Patent or Trademark Office should be transacted in writing. The personal attendance of applicants or their attorneys or agents at the Patent and Trademark Office is unnecessary. The action of the Patent and Trademark Office will be based exclusively on the written record in the Office. No attention will be paid to any alleged oral promise, stipulation, or understanding in relation to which there is disagreement or doubt.

The action of the Patent and Trademark Office cannot be based exclusively on the written record in the Office if that record is itself incomplete through the failure to record the substance of interviews.

It is the responsibility of the applicant or the attorney or agent to make the substance of an interview of record in the application file, unless the examiner indicates he or she will do so. It is the examiner's responsibility to see that such a record is made and to correct material inaccuracies which bear directly on the question of patentability.

Examiners must complete an Interview Summary Form for each interview held where a matter of substance has been discussed during the interview by checking the appropriate boxes and filling in the blanks. Discussions regarding only procedural matters, directed solely to restriction requirements for which interview recordation is otherwise provided for in Section 812.01 of the Manual of Patent Examining Procedure, or pointing out typographical errors or unreadable script in Office actions or the like, are excluded from the interview recordation procedures below. Where the substance of an interview is completely recorded in an Examiners Amendment, no separate Interview Summary Record is required.

The Interview Summary Form shall be given an appropriate Paper No., placed in the right hand portion of the file, and listed on the "Contents" section of the file wrapper. In a personal interview, a duplicate of the Form is given to the applicant (or attorney or agent) at the conclusion of the interview. In the case of a telephone or video-conference interview, the copy is mailed to the applicant's correspondence address either with or prior to the next official communication. If additional correspondence from the examiner is not likely before an allowance or if other circumstances dictate, the Form should be mailed promptly after the interview rather than with the next official communication.

The Form provides for recordation of the following information:
- Application Number (Series Code and Serial Number)
- Name of applicant
- Name of examiner
- Date of interview
- Type of interview (telephonic, video-conference, or personal)
- Name of participant(s) (applicant, attorney or agent, examiner, other PTO personnel, etc.)
- An indication whether or not an exhibit was shown or a demonstration conducted
- An identification of the specific prior art discussed
- An indication whether an agreement was reached and if so, a description of the general nature of the agreement (may be by attachment of a copy of amendments or claims agreed as being allowable). Note: Agreement as to allowability is tentative and does not restrict further action by the examiner to the contrary.
- The signature of the examiner who conducted the interview (if Form is not an attachment to a signed Office action)

It is desirable that the examiner orally remind the applicant of his or her obligation to record the substance of the interview of each case unless both applicant and examiner agree that the examiner will record same. Where the examiner agrees to record the substance of the interview, or when it is adequately recorded on the Form or in an attachment to the Form, the examiner should check the appropriate box at the bottom of the Form which informs the applicant that the submission of a separate record of the substance of the interview as a supplement to the Form is not required.

It should be noted, however, that the Interview Summary Form will not normally be considered a complete and proper recordation of the interview unless it includes, or is supplemented by the applicant or the examiner to include, all of the applicable items required below concerning the substance of the interview.

A complete and proper recordation of the substance of any interview should include at least the following applicable items:
1) A brief description of the nature of any exhibit shown or any demonstration conducted,
2) an identification of the claims discussed,
3) an identification of the specific prior art discussed,
4) an identification of the principal proposed amendments of a substantive nature discussed, unless these are already described on the Interview Summary Form completed by the Examiner,
5) a brief identification of the general thrust of the principal arguments presented to the examiner,
   (The identification of arguments need not be lengthy or elaborate. A verbatim or highly detailed description of the arguments is not required. The identification of the arguments is sufficient if the general nature or thrust of the principal arguments made to the examiner can be understood in the context of the application file. Of course, the applicant may desire to emphasize and fully describe those arguments which he or she feels were or might be persuasive to the examiner.)
6) a general indication of any other pertinent matters discussed, and
7) if appropriate, the general results or outcome of the interview unless already described in the Interview Summary Form completed by the examiner.

Examiners are expected to carefully review the applicant's record of the substance of an interview. If the record is not complete and accurate, the examiner will give the applicant an extendable one month time period to correct the record.

Examiner to Check for Accuracy

If the claims are allowable for other reasons of record, the examiner should send a letter setting forth the examiner's version of the statement attributed to him or her. If the record is complete and accurate, the examiner should place the indication, "Interview Record OK" on the paper recording the substance of the interview along with the date and the examiner's initials.